PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sharing and re-use of individual participant data from clinical trials: Principles and recommendations
AUTHORS	Ohmann, Christian; Banzi, Rita; Canham, Steve; Battaglia, Serena; Matei, Mihaela; Ariyo, Christopher; Becnel, Lauren; Bierer, B; Bowers, Sarion; Clivio, Luca; Dias, Monica; Druml, Christiane; Faure, Hélène; Fenner, Martin; Galvez, Jose; Gershi, Davina; Gluud, Christian; Groves, Trish; Houston, Paul; Ghassan, Karam; Kalra, Dipak; Knowles, Rachel; Krleža-Jerić, Karmela; Kubiak, Christine; Kuchinke, Wolfgang; Kush, Rebecca; Lukkarinen, Ari; Marques, Pedro; Newbigging, Andrew; O'Callaghan, Jennifer; Ravaud, Philippe; Schlünder, Irene; Shanahan, Daniel; Sitter, Helmut; Spalding, Dylan; Tudur-Smith, Catrin; van Reusel, Peter; van Veen, Evert-Ben; Visser, Gerben Rienk; Wilson, Julia; Demotes, Jacques

VERSION 1 – REVIEW

REVIEWER	Sean Coady National Heart, Lung, and Blood Institute
REVIEW RETURNED	13-Aug-2017

GENERAL COMMENTS	The report is a comprehensive consensus concerning the wide sharing of clinical trial data. The consensus report covers ten principles and 50 recommendations on a framework for sharing trial data. The report is very well written and provides a unique set of comprehensive principles for developing an approach to data sharing from trials. The report indicates that "the emphasis throughout has been on the perspective of clinical researchers, considered both as data generators and as data requesters". The term 'data generators' may not be well received. The term, by and of itself, could be construed as 'mildly disrespectful' as the initial reaction would be 'generating data for others to use' rather than as trialists, that propose, develop, monitor, and conduct complex trials. Along these lines, at least one principle should recognize the intellectual contributions of the original trialists. I realize that some of the recommendations address 'data generators'; however, it is disappointing that none of the principles concern recognizing the original trialists. While the focus is on sharing trial data and trial objects widely, recognition should be given to the potential benefits of sharing using both internal data sharing processes (for example, collaboration utilizing a study publication committee) and wide sharing. Collaborators, utilizing original study investigators, gain key insights into study nuances and internal study review can substantially enhance the quality of the work.

	The concept of stewardship versus ownership may not have been fully explored by the group. Ownership and rights to data is a complex legal issue that may need to be explored further. Recommendation 18 concerning residual risks for re-identification is a little vague. It is unclear from the document just how these risk assessments should take place. Are tools or guidelines available that actually quantify risk or is risk assessment largely a judgement call? The report was particularly useful in describing where major disagreements occurred in the drafting of the principles and recommendations. Areas of concerns or disagreements should be areas in which potential empirical data are needed. Nearly all of the principles are based on opinion, further evidence gathering should be a priority. An expansion of the section on the need for empirical research is warranted..

REVIEWER	Prof Rod Taylor University of Exeter Medical School I am currently undertaking an NIHR HTA programme funded IPD meta-analysis
REVIEW RETURNED	16-Aug-2017

GENERAL COMMENTS	This is an important paper undertake under the umbrella of ECRIN that comprehensively assesses the key issues the sharing IPD and makes recommendations for researchers, research funders, and other key stakeholders. My only two comments are 1. The paper is presented as a report format that does readily conform with format of a journal paper and I would suspect needs reformatting - I will leave this with the journal editors 2. relatedly, the methods section currently seems very short. A more detailed description is needed to allow the review to appraise the robustness of the methodology undertaken.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1, Reviewer Name: Sean Coady

Comment 1. Trialist/data generator
The report indicates that "the emphasis throughout has been on the perspective of clinical researchers, considered both as data generators and as data requesters". The term 'data generators' may not be well received. The term, by and of itself, could be construed as 'mildly disrespectful' as the initial reaction would be 'generating data for others to use' rather than as trialists, that propose, develop, monitor, and conduct complex trials. Along these lines, at least one principle should recognize the intellectual contributions of the original trialists. I realize that some of the recommendations address 'data generators'; however, it is disappointing that none of the principles concern recognizing the original trialists.

Response: We understand the reviewer concerns about the terminology “data generator” and we revised some parts of the text to make clear that we did not use ‘data generators’ in any derogatory sense.

At the top of page 7, ‘data generators’ has been replaced by ‘trialists’.
On page 8, the perspective of the researcher has been expanded, splitting the first paragraph up and extending it to try and ensure we are not using ‘data generators’ in any derogatory sense.
Unfortunately, the wording of the principles and the recommendations could not be changed as this would require further rounds of discussions by the consensus conferences. Even if there is no specific principle explicitly dedicated to trialists, we believe the respect and acknowledgment of their contributions are covered by principle 1 and the corresponding recommendations.
Glossary p. 68, no. 21, a comment was added.

Comment 2. Involvement of data generators in secondary use
While the focus is on sharing trial data and trial objects widely, recognition should be given to the potential benefits of sharing using both internal data sharing processes (for example, collaboration utilizing a study publication committee) and wide sharing. Collaborators, utilizing original study investigators, gain key insights into study nuances and internal study review can substantially enhance the quality of the work.

Response: 33, page 32: We have tried to emphasise the potential benefits from involving primary researchers in data sharing more clearly in the text.

Comment 3. Stewardship versus ownership
The concept of stewardship versus ownership may not have been fully explored by the group. Ownership and rights to data is a complex legal issue that may need to be explored further.

The point raised by the reviewer is relevant; however, the details of the legal issues that surround these concepts were deemed to technical and context-dependent to be covered in this consensus exercise.

Response: 2, page 14. The issue of data ownership versus data stewardship has been explored further in the text by adding a paragraph. As we try to make clear, however, there was a clear statement by the consensus group to keep clear of these more legal and technical issues and to tackle this delicate problem in the future.

Comment 4. Tools/guidelines for risk-estimation
Recommendation 18 concerning residual risks for re-identification is a little vague. It is unclear from the document just how these risk assessments should take place. Are tools or guidelines available that actually quantify risk or is risk assessment largely a judgement call?

Response: 18 (page 25): A paragraph was added, referring to practical guidance on managing de-identification and quantitatively assessing associated risks (IOM, Appendix B, 2015; Article 29 WP, 2017).

Comment 5. Empirical evidence
Nearly all of the principles are based on opinion, further evidence gathering should be a priority. An expansion of the section on the need for empirical research is warranted.

Response: We agree with the reviewer that the paucity of empirical data on standards and practice for clinical trial data sharing calls for further multifaceted research activities.

Discussion, pages 46-47: We have expanded the text by referring to the limited number of existing empirical studies (with some examples) and have pointed out that because our principles and recommendations are consensus-based, further evidence gathering should be a priority.

Reviewer: 2, Reviewer Name, Prof Rod Taylor

Comment 6. Format of the paper
The paper is presented as a report format that does readily conform with format of a journal paper and I would suspect needs reformatting - I will leave this with the journal Editors

Response: We understand the current format is not standard but we discussed the issue with the editor who confirmed that is acceptable.

Comment 7. Detailed description of methodology
Relatedly, the methods section currently seems very short. A more detailed description is needed to allow the review

Response: Methods, page 9: The methodological approach has been expanded with a detailed description of all steps of the consensus process. In addition, a further reference was added.